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In re Application of

GLENN ALBRECHT

Application Number

081 862,610

Filed

MAY 23, 1997

Paper No.

#7

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US006013445A

# United States Patent [19]

Albrecht et al.

[11] Patent Number: 6,013,445  
[45] Date of Patent: Jan. 11, 2000

[54] MASSIVELY PARALLEL SIGNATURE SEQUENCING BY LIGATION OF ENCODED ADAPTORS

[75] Inventors: Glenn Albrecht, Redwood City, Calif.; Sydney Brenner, Cambridge, United Kingdom; Robert B. DuBridge, Belmont, Calif.; David H. Lloyd, Daly City, Calif.; Michael C. Pallas, San Bruno, Calif.

[73] Assignee: Lynx Therapeutics, Inc., Hayward, Calif.

[21] Appl. No.: 08/946,138

[22] Filed: Oct. 7, 1997

## Related U.S. Application Data

[63] Continuation-in-part of application No. 08/862,610, May 23, 1997, abandoned, which is a continuation-in-part of application No. 08/689,587, Aug. 12, 1996, abandoned, which is a continuation-in-part of application No. 08/659,453, Jun. 6, 1996, abandoned.

[51] Int. Cl.<sup>7</sup> ..... C12Q 1/68; C07H 21/02

[52] U.S. Cl. .... 435/6; 536/24.2

[58] Field of Search ..... 435/6, 91.52; 536/24.2, 536/24.3, 26.6; 935/77, 78

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Primary Examiner—Eggerton A. Campbell  
Attorney, Agent, or Firm—Stephen C. Macevitz

## [57] ABSTRACT

The invention provides a method of nucleic acid sequence analysis based on the ligation of one or more sets of encoded adaptors to the terminus of a target polynucleotide. Encoded adaptors whose protruding strands form perfectly matched duplexes with the complementary protruding strands of the target polynucleotide are ligated, and the identity of the nucleotides in the protruding strands is determined by an oligonucleotide tag carried by the encoded adaptor. Such determination, or "decoding" is carried out by specifically hybridizing a labeled tag complement to its corresponding tag on the ligated adaptor.

29 Claims, 10 Drawing Sheets